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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,394	08/05/2005	Jonathan S Stamler	28195-508 NATL	2192

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EXAMINER	
SZNAIDMAN, MARCOS L	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,394	STAMLER ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7 and 8* is/are pending in the application.

4a) Of the above claim(s) *7 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on January 14, 2009.

Status of Claims

Cancellation of claims 2-6 and amendment of claim 1 is acknowledged.

Claims 1 and 7-8 are currently pending and are the subject of this office action.

Claim 7-8 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 22, 2008.

Claim 1 are presently under examination.

Priority

The present application is a 371 of PCT/US02/36138 filed on 12/02/2002, and claims priority to provisional application No. 60/336,175 filed on 12/06/2001.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (New Rejection Necessitated by Amendment)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kreidstein et. al. (CAS accession # 1993:1375, corresponding to Canadian Journal of Physiology and Pharmacology (1992) 70:1208-1216, cited in prior office action) in view of Cederqvist et. al. (CAS accession # 1994:289800, corresponding to Biochemical Pharmacology (1994), 47:1047-1053, cited in prior office action).

Claim 1 recites a method for preventing necrosis in a pedicle flap or in any microvascular surgery, comprising topically applying to pedicle or other source of blood supply, a therapeutically effective amount of a vasodilator composition comprising ethyl nitrite.

For claim 1, Kreidstein et. al. teach the potential use of topical nitrovasodilators or NO donors for prevention and (or) treatment of skin flap ischemia (i.e. ischemic necrosis) (see abstract, last 4 lines).

Kreidstein et. al. do not teach the use of ethyl nitrite. However, Cederqvist et. al. teach that Ethyl nitrite and organic nitrites in general are NO donors (see abstract).

Since Kreidstein teaches a method of treating or preventing skin flap necrosis with a NO donor, and since Cederqvist teaches that ethyl nitrite is a NO donor, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any NO donor) for another (ethyl nitrite) with an expectation of success, since the prior art establishes that both function

in similar manner, thus resulting in the practice of claim 1, with a reasonable expectation of success.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Davies et. al. (CAS accession # 1998:302984, corresponding to Annals of Plastic Surgery (1998) 40:630-636, cited in prior office action); in view of Cederqvist et. al. (CAS accession # 1994:289800, corresponding to Biochemical Pharmacology (1994), 47:1047-1053, cited in prior office action).

Claim 1 recites a method for preventing necrosis in a pedicle flap or in any microvascular surgery, comprising topically applying to pedicle or other source of blood supply, a therapeutically effective amount of a vasodilator composition comprising ethyl nitrite.

For claim 1, Davies et. al. teach that nitroglycerin (a NO donor) improves random-pattern skin flap survival significantly after mainstream cigarette smoke exposure in the rat. These results imply that pharmacological intervention with vasodilators may ultimately prove clinically useful for random-pattern skin flap salvage in the cigarette-smoking patient (see abstract).

Davies et. al. do not teach the use of ethyl nitrite. However, Cederqvist et. al. teach that Ethyl nitrite and organic nitrites in general are NO donors (see abstract).

Since Davies teaches a method of treating or preventing skin flap necrosis with a NO donor, and since Cederqvist teaches that ethyl nitrite is a NO donor, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any NO donor) for another (ethyl nitrite)

with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claim 1, with a reasonable expectation of success.

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues there is no objective reason provided by any of the cited references, alone or in combination that would lead the skilled artisan to use ethyl nitrite to prevent flap necrosis.

Examiner's response: see above rejection.

Applicant further argues: the present invention provides superior properties not taught or suggested by the combination of references cited by the Examiner. Specifically, as shown in detail in the present specification at Example 1, topical application of ethyl nitrite to a vasoconstricted pedicle flap caused greater restoration of blood flow and had a longer lasting effect on arterial dilation and blood flow as compared to the art recognized vasodilator lidocaine (see Specification at page 7, lines 12-17).

Examiner's response: the results of example 1 do not show any unexpected results. For example: arterial vasodilation for lidocaine after 30 min is 82+/-6%, and for ethyl nitrite is 98+/-5%; lidocaine increased the blood flow to 55+/-7% after 30 min., while ethyl nitrite increased to 86+/-10% after 30 min. So even though there are differences, these are not unexpected because they fall within the normal statistical variation in the art. Also, applicant provided comparison data for only one set of

concentrations, and the concentrations used are not the same: 2% lidocaine and 10-4 M for ethyl nitrite, so there is no way to know if the differences are real or the result of using different concentrations. In order to claim unexpected results, applicant should provide a wide range of concentrations for both ingredients and then compare the results.

Withdrawn Rejections and/or Objections

Claim 1 previously rejected under 35 USC 103 (a)

Due to applicant's amendment of claim 1 the 35 USC 103(a) rejection is now moot. Rejection under 35 USC 103 (a) is withdrawn.

However, a new rejection under 35 USC 103 (a) necessitated by amendment (see above) was applied.

Claims 2-6 previously rejected under 35 USC 103 (a)

Due to applicant's cancellation of claims 2-6 the 35 USC 103(a) rejection is now moot.

Rejection under 35 USC 103 (a) is withdrawn.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
March 12, 2009

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612